REMARKS

Status of the Claims

Claims 1-4, 6-7, 9-12, 15, 17-18, 33, 36, 42-44 and 46-55 were pending in the present application.

Claims 1-4, 6-7, 9-12, 15, 17-18, 33, 36, 42-44 and 46-55 were rejected.

By way of this amendment, claim 33 has been amended, claims 44, 46, 48 and 51 have been canceled and new claims 56-58 have been added.

Upon entry of this amendment, claims 1-4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42, 43, 47, 49, 50 and 52-58 will be pending.

Summary of the Amendment

Claims 33 has been amended to more clearly set forth specific embodiments of the invention more precisely. Support for the amendments appears throughout the specification and claims as originally filed.

Claims 44, 46, 48 and 51 have been canceled.

New claims 56-58 have been added to refer to embodiments of the invention. Support for the amendments appears throughout the specification and claims as originally filed.

No new matter has been added.

Claim Objections

Claims 1-4, 6-7, 9-12, 15, 17-18, 33, 36, 42-44 and 46-55 stand rejected as reciting non-elected subject matter. Applicants respectfully note that each of the claims read on the elected species. Upon concluding that the elected species is allowable, Applicants respectfully request

that the generic claims which read on the elected species and a reasonable number of non-elected species be examined and allowed.

Claim Rejections Based Upon 35 U.S.C. §112, first paragraph

Claims 1-4, 6-7, 9-12, 15, 17-18, 33, 36, 42-44 and 46-55 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing the enablement requirement. The Office asserts that it would have required undue experimentation to practice the scope of the invention as claimed. The Office asserts that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The Office asserts that the unpredictability in the art provides the basis to doubt Applicants' assertions of enablement. Applicants respectfully disagree.

Applicants note that claim 33 has been amended to refer to "a plasmid" as the delivery vehicle of the nucleic acid sequences encoding the immunogen and the immunomodulating protein.

The official action states that the specification is enabling for

> 1) a method of immunizing a mammal against influenza comprising co-admininstering a plasmid encoding Influenza HA and a plasmid encoding DR5 by muscular injection and 2) a pharmaceutical composition compring a plasmid encoding Influenza HA and a plasmid encoding DR5.

(Paragraph bridging pages 3 and 4 of Official Action dated April 2, 2008.) Accordingly, claims 46, 47, 49, 50 and 52 are enabled. Claims 49 and 50 correspond to the subject matter indicated as enabled. Claims 46, 47 and 52 differ from claims 49 and 50 in that claims 46, 47 and 52 include both coding sequences on a single plasmid. There is no basis to support a finding that the presence of both coding sequences on a single plasmid is unpredictable relative to the embodiments in which the coding sequences are on separate plasmids.

With regard to claims 1-4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42-44 and 53-55, Applicants respectfully urge that the a person skilled in the art would accept applicants assertions of enablement with respect to the claimed subject matter.

It is asserted that one skilled in the art would not accept the evidence of record to conclude that the combination of coding sequences encoding DR5 and an immunogen other than Influenza HA could be predicted to effect B cells and that generation of antigen specific CD8+ T cells does not correlate to an antiviral effect. Moreover, it is asserted that one skilled in the art would not conclude that the combination of coding sequences encoding DR5 and an immunogen other than Influenza HA could be predicted to generate antigen specific CD8+ T cells.

The Official Action states that in view of 1) the state of the art in generating therapeutic immune responses at the time of filing; 2) the lack of specific guidance for using DR5 to enhance immune responses, 3) the limited data in the declaratory evidence, and the unpredictability in immunizing against any pathogenic disease by generating a CD8+ response and 4) he breadth of the claims, it would have required undue experimentation to practice the scope of the invention as claimed. Applicants respectfully point out that the method claims 7, 11, 18, 33 and 36 set forth methods of "inducing cytotoxic T cell" responses. These methods are enabled.

Based upon the state of the art at the time of filing, one skilled in the art could generate immune responses as claimed using DNA vaccine technology following the teachings of the specification. There is nothing in the record to support a conclusion that the use of DNA vaccines to generate cytoxic T cell responses as claimed was unpredictable. The data show that DR5 further enhances such immune responses.

With respect to "the lack of specific guidance for using DR5 to enhance immune responses" the methods of using DR5 have been clearly and adequately set forth. Based upon the entire record, one skilled in the art would be able to use DR5 and would accept Applicants assertions that its use would provide enhanced immune responses. The specification provides

clear guidance with respect to practicing the invention. The data show that DR5 has adjuvant properties when used as part of a DNA vaccine protocol. At the time of the invention, one skilled in the art could make and use DNA vaccines, and the specification describes how DR5 can be incorporated to improve such vaccines.

The Office relies upon Yasumoti et al., Erdile et al and Ertl et al. to support the conclusion that generation of antigen specific CD8+ T cells does not correlate to effective protective antiviral activity. While not every CD8+ immune response will result in protective immunity, Applicants maintain that one skilled in the art could reasonably predict that a cytotoxic T cell response against an immunogen can be generated in an individual by administering to the individual by intramuscular injection: a composition comprising one plasmid or more than one plasmid which comprise a nucleotide sequence that encodes said immunogen operable linked to regulatory elements; and a nucleotide sequence that encodes said DR5 as claimed. One skilled in the art would recognize that such an immune response can be generated against and immunogen and that the immune response will be enhanced by the inclusion of DR5 coding sequences. Applicants urge that the degree to which the immune response is protective is not an element required by the claims. As pointed out by the Office, not all cytotoxic T cells responses against pathogen antigens will protect against pathogen infection. However, the claim does not refer to protective immune responses. Moreover, cytotoxic T cells responses may provide antiviral activities despite not providing protection against infection of naïve individuals.

In view of the evidence of record, those having ordinary skill in the art would conclude that the claimed invention is enabled. Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

Claim Rejections Based Upon 35 U.S.C. §102

Claims 1, 6, 12, 53 and 54 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent number 6,417,328 (hereinafter "Alnemri"). Applicants respectfully disagree and request that the rejection based upon 35 U.S.C. § 102(e) be withdrawn.

Alnemri does not anticipate any of claims 1, 6, 12, 53 and 54. The claims refer to "pyrogen-free" compositions." Alnemri does not recite "compositions that are pyrogen free which include nucleic acid sequences that encode DR5 and an immunogen." The Office asserts that the passage in Alnemri which refers to therapeutics which comprise DR5 in a physiological carrier applies to the passages in Alnemri disclosing laboratory reagents that include nucleic acid sequences that encode DR5 and an immunogen. One skilled in the art reading Alnemri clearly conclude that the passage referring to physiological carriers has nothing to do with the compositions disclosed elsewhere in the documents which are provided as reagents for experiments. One skilled in the art would not expect that the compositions disclosed in the document as reagents for experiments would be pyrogen free. The removal of pyrogens is an expensive, arduous task which is not generally necessary and thus not typically performed to produce the grade of reagent disclosed in the reference. Pyrogen removal is generally associated with human therapeutics which is the context in which Alnemri was describing physiological carriers for contemplated therapeutics. Alnemri neither teaches nor suggests using a combination of nucleic acid sequences that encode DR5 and an immunogen as a therapeutic composition.

It is well established that to anticipate a claim, the prior art reference must describe the invention. That is, the art must disclose the elements "arranged as in the claim" See Net MoneyIN, Inc. v. VeriSign, Inc., 545 F.3d 1359, 1369 (Fed. Cir. 2008). As stated in In re Arkley, 455 F.2d 586, 587 (C.C.P.A. 1972), cited in Net MoneyIN:

> [The] reference must clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference.

Alnemri does not disclose the claim invention. Reference to the elements of the claim relied upon by the Office are found in different parts of the disclosure which are unrelated. Alnemri disclosure of discrete elements listed in the claim is not a disclosure of the invention. The case for anticipation as provided by the Office violates the well settle law with respect to disclosure of elements of a claim found in disparate parts of a disclosure which does not disclose the invention.

In view of the foregoing, Applicants respectfully request that the rejections of claims 1, 6, 12, 53 and 54 under 35 U.S.C. § 102(e) as being anticipated by Alnemri be withdrawn.

Claim Rejections Based Upon 35 U.S.C. §103

Claims 1, 6, 12, 53 and 54 stand rejected under 3 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Alnemri in view of US Pat. No. 5,693,622 (hereinafter "Wolff").

As noted above, Alnemri does not disclose pyrogen free compositions comprising nucleic acid sequences that encode DR5 and an immunogen

Nothing in Wolff, which discloses delivery of DNA vaccines, teaches or suggests the inclusion of DR5 enciding DNA in a pyrogen free composition.

The combination of references do not yield the invention . The combination of references do not provide pyrogen free compositions comprising nucleic acid sequences that encode DR5 and an immunogen nor does the combination provide any suggestion to modify the references to produce such a combination of elements.

Applicants respectfully request that the rejection based upon 35 U.S.C. §103(a) be withdrawn.

Conclusion

Claims 1-4, 6, 7, 9-12, 15, 17, 18, 33, 36, 42, 43, 47, 49, 50 and 52-58 are in condition for allowance. A notice of allowance is earnestly solicited. The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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